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Self-help Cognitive Behavioral Therapy Improves Health-Related Quality of Life for Inflammatory Bowel Disease Patients: A Randomized Controlled Effectiveness Trial

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Abstract
Patients with inflammatory bowel disease (IBD) often have poor health-related quality of life (HRQL) and are at risk for anxiety and depression. Cognitive behavioral therapy (CBT) can help patients with IBD cope with their disease. Unfortunately, barriers to care include expense and availability of qualified therapists. Stand-alone, self-help CBT could improve access to care. This study examined the effectiveness of a self-help CBT workbook for patients with IBD. A randomized controlled trial compared the CBT workbook to an active psychoeducational control workbook. A total of 140 participants enrolled. In both groups, scores improved on a range of measures, including catastrophizing, visceral sensitivity, and HRQL, although pre-post effect sizes were generally larger in the CBT group. Only participants in the CBT group experienced significant improvements in anxiety and depression. Improvements were generally maintained or consolidated at 3-month follow-up. Self-help CBT can be an effective and inexpensive way to improve HRQL for patients with IBD.

Keywords Crohn's disease · Ulcerative colitis · Inflammatory bowel disease · Cognitive-behavioral therapy · Self-help · Health-related quality of life

Introduction

Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), significantly impairs an individual's health-related quality of life (HRQL) (Zhou, Ren, Irvine, & Yang, 2010). Unlike functional GI disorders such as irritable bowel syndrome (IBS), IBDs are autoimmune disorders that can result in significant physical disability and even life-threatening emergencies (Burisch, Jess, Martinato, & Lakatos, 2013). Indeed, up to 80% of patients with Crohn's disease will require corrective surgery at some point in their life (Sica & Biancone, 2013). In addition, individuals who have IBD are much more likely to suffer from anxiety and depression compared with the general population (Goodhand et al., 2012; Graff, Walker, & Bernstein, 2009; Kovacs & Kovacs, 2007), with individuals with active disease being particularly at risk (Mikocka-Walus, Knowles, Keefer, & Graff, 2016). The existence of a comorbid psychological disorder further reduces HRQL in individuals with IBD regardless of the medical severity of their condition (Guthrie, 2002; Iglesias-Rey et al., 2014).

The relationship between psychological distress and disease activity appears to be bidirectional. Psychological distress may be a response to disease activity itself (Sewitch, 2001), and long-term stress and depression may also worsen or exacerbate the disease (Bernstein, Singh, Graff, Walker, & Cheang, 2011; Graff et al., 2009; Levenstein, 2000; Maunder & Levenstein, 2008). For example, Persoons et al. (2005) found that major depressive disorder was predictive of failure to achieve remission while using infliximab for the medical management of CD. Bitton et al. (2009) showed that psychosocial variables, including high levels of perceived stress, especially in combination with avoidant coping, as well as biological markers, predicted relapse in patients with IBD. Mittmaier et al. (2004) reported that scores on the Beck Depression Inventory correlated with the number of relapses at the 18-month follow-up. Mikocka-Walus, Pittet, Rossel, and von Känel (2016) found a significant association

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between symptoms of depression or anxiety and clinical recurrence. They strongly suggested that patients with IBD should be screened for clinically significant distress and referred to mental health practitioners for further evaluation and treatment.

There are a number of mechanisms by which stress and distress can affect inflammation, including hypothalamic–pituitary axis dysfunction, alterations in bacterial–mucosal interactions, effects on mucosal mast cells and mediators such as corticotrophin-releasing factor (Bonaz & Bernstein, 2013; Mawdsley & Rampton, 2005, 2006). In addition, psychological distress is strongly related to *perceived* health in patients with IBD over and above actual disease severity (Gracie & Ford, 2017; Graff, Walker, Clara et al., 2009; Sexton et al., 2017). Thus, the assessment and treatment of psychological disorders in this population are likely to result in an improvement of HRQL. Indeed, most international guidelines for the management of IBD call for attention to psychosocial issues and psychological distress (Häuser, Moser, Klose, & Mikocka-Walus, 2014).

Cognitive-behavioral therapy (CBT) is one of the psychosocial treatments with the most evidence supporting its efficacy in the treatment of patients with IBD (Knowles, Monshat, & Castle, 2013; von Wietersheim & Kessler, 2006). Mussell, Böcker, Nagel, Olbrich, and Singer (2003) found that group CBT could be effective for both short-term and long-term management of psychological distress in patients with IBD. Everstz et al. (2012) developed a manualized CBT treatment for patients with IBD with the goal of improving HRQL. In a definitive efficacy trial, Mikocka-Walus et al. (2015) tested the effects of face-to-face CBT or online CBT compared to standard treatment alone on disease activity and quality of life in patients with IBD in a rigorous, 24-month longitudinal study. Although CBT did not affect objective measures of inflammation (Mikocka-Walus et al., 2017), the treatment did result in significant improvement in HRQL in the particular subgroups who were most in need of treatment. Importantly, the trial did not find many significant differences between the efficacy of online CBT and the face-to-face CBT. A recent review and meta-analysis (Gracie et al., 2017) found that psychological therapy, and CBT in particular, had beneficial effects on both depression and quality of life in patients with IBD, but no impact on objective disease severity.

Unfortunately, the psychological concomitants and comorbidities of IBD often remain untreated (Evertsz', Bockting et al. 2012; Evertsz', Thijssens et al. 2012), despite the strong evidence for the value of adding psychological interventions to standard medical care (Sajadinejad, Asgari, Molavi, Kalantari, & Adibi, 2012; Szigethy et al., 2017). That is, although CBT has demonstrated *efficacy* in a number of well-done studies, most patients with IBD are not getting any psychological help, much less empirically supported help like CBT. One study of the experiences of patients with IBD (Craven, Quinton, & Taft, 2018) suggested that many patients desire psychotherapy and perceive it as helpful, but that there is a significant disparity between their desires for mental health treatment and their actual interactions with providers. Cost and the dearth of IBD-knowledgeable therapists were identified as the primary barriers to care.

This gap between the existence of well-controlled clinical trials and real-world dissemination and adoption of interventions is a problem throughout the health care world, and has been labeled the efficacy-to-effectiveness transition (Glasgow, Lichtenstein, & Marcus, 2003). An efficacy trial is characterized by strong controls, delivering a standardized program to a specific, often narrowly defined, homogeneous target group. Effectiveness trials, in contrast, are designed to test whether an intervention works in the real world for a broadly defined population (Flay, 1986). In addition to ongoing efficacy trials, we also need *effectiveness* trials, which test the performance of interventions, including interventions with GI patients specifically, under real-world conditions (Singal, Higgins, & Waljee, 2014). As Singal et al. (2014) point out, effectiveness studies maximize external validity, more closely approach real-world practice, and allow more heterogeneous patient populations, brief, feasible interventions, and delivery across multiple settings.

Fortunately, CBT is particularly amenable to modularized, computerized, and self-help-based intervention strategies, which are easy to export in effectiveness trials and real-world settings (Williams & Martinez, 2008). Self-help books are as easy for patients to obtain as clicking a "buy now" button on an online book retailer's website and are therefore broadly available. Moreover, self-help CBT may well be as effective overall as in-person therapy (King, Orr, Poulsen, Giacomantonio, & Haden, 2017). Self-help interventions are much less expensive than standard CBT therapy and much more accessible, thus overcoming many of the barriers to care cited by patients with IBD (Craven et al., 2018). Moreover, studies have shown that self-help psychosocial interventions can be quite effective in reducing anxiety, depression, and distress in patients suffering from physical illnesses (Matcham et al., 2014), including functional GI disorders like IBS (Hunt, Ertel, Coello, & Rodriguez, 2014a). However, a vast majority of self-help books are never tested at all (Rosen, 1993), and while some are based on empirically supported principles and treatments, it is the very rare book that is itself directly tested in any sort of clinical trial (Norcross, 2000).

McCombie, Gearry, Andrews, Mulder, and Mikocka-Walus (2016) tested a computerized self-help program based on CBT principles for patients with IBD. Treatment completers showed improvement at 12 weeks, but those gains were not maintained at 6 months. Unfortunately, the study suffered from significant attrition, with only 26% of participants assigned to the CBT

intervention actually completing at least half of the intervention modules.

Hunt, Rodriguez, and Marcelle (2017) tested the efficacy of a CBT self-help workbook, delivered online with minimal therapist feedback for patients with IBD. Participants, all of whom had IBD, were randomized to either the treatment condition or a waitlist control group. The treatment group reported improvement in HRQL and anxiety about visceral sensations, as well decreases in catastrophizing and in depressive symptoms (Hunt et al., 2017). Subsequent to that trial, the workbook was significantly revised and expanded. The manuscript was shared with a number of stakeholders, including patients with IBD, who provided constructive feedback and suggested edits and additions. In particular, many clinical examples were added, as well as chapters on ostomies and medical management. The revised book was designed to serve as a stand-alone self-help book, requiring no therapist intervention or feedback.

The current study is a randomized controlled effectiveness trial comparing the revised self-help workbook, titled *Coping with Crohn's and Colitis,* to an active psychoeducational control workbook. Despite the fact that effectiveness trials typically compare the active intervention to usual care or waitlist, rather than a placebo (Singal et al., 2014), we decided to employ a stronger design on the spectrum between a tightly controlled efficacy trial and a more externally valid effectiveness trial. The psychoeducational workbook was developed by compiling articles from various online sites that are publicly accessible, such as WebMD, Mayo Clinic, Crohn's and Colitis Foundation (CCF), and others.

We hypothesized that the self-help group would show significant improvements compared to the psychoeducational group in terms of anxiety, depressive symptoms, anxiety about visceral sensations, catastrophizing, and HRQL. However, we did not anticipate that either group would display a significant improvement in disease symptom severity compared to baseline.

Methods

This study was approved by the Institutional Review Board at the University of Pennsylvania. We obtained active and informed consent from all participants prior to their completing the intake questionnaires. The trial was not registered with a trial registry, but was advertised on the clinical trials page of the Crohn's and Colitis Foundation.

Design

The study was a 2-arm, parallel randomized controlled effectiveness trial with cross over from the control condition to the active treatment arm offered at 6 weeks.

Participants

Eligibility for the study consisted of patient report that they had been diagnosed by a physician with IBD. Disease did not have to be active at the time of enrollment. A subset ($n = 38$, 27%) of participants were referred to the study by their gastroenterologist, an expert in IBD, who confirmed the diagnosis. A total of 140 subjects were enrolled (93 female, 47 male). Sample size was determined based on similar trials (e.g., Hunt et al., 2017; Mikocka-Walus et al., 2015), and anticipating approximately 50% attrition, which is standard in self-help, internet trials (Mathieu, McGeechan, Barratt, & Herbert, 2013). Power calculations (based on BDI scores from Hunt et al., 2017) suggested that for 80% power and 5% Type 1 error, we required 29 participants per group. Allocating 140 individuals to treatment, with 50% attrition, would yield 35 individuals per group and should provide sufficient power to detect moderate effects.

Participants were randomized to condition using the coin flip available from random.org. Participants were allocated upon receipt of their consent and confirmation of eligibility by a research assistant, who assigned sequential participants based on the results of the coin toss. Thus, allocation was not predetermined and was concealed until assignment. Participants then received an email informing them of their group allocation and including a link to the first module of their assigned book. Seventy participants were randomized to the CBT-based self-help workbook, while 70 participants were randomized to the active psychoeducational control group.

Sixty-seven subjects suffered from CD, 49 subjects from UC, and 24 subjects did not specify. A total of 19 subjects (14%) also indicated a comorbid, secondary irritable bowel syndrome (IBS) diagnosis. Ages ranged from 18 to 79 years old (mean 35.34, standard deviation [SD] 13.18 years). The racial distribution of the sample was as follows: 88% White, 2% Black or African American, 1.5% Hispanic, 1% American Indian/Alaskan Native, 4% Asian, 2% biracial, and 1.5% reporting other races. See Table 1 for a full accounting of participant characteristics. Administration of the Harvey Bradshaw Index, a validated disease activity index for CD, at recruitment revealed that 2% of patients reported severe disease activity, 53% of patients reported moderate disease activity, 30% of patients reported mild disease activity, and 15% of patients reported being in remission.

Subjects were recruited online and in-person between October of 2015 and January of 2017. Final follow-up data were obtained from the last subject in July of 2017. Online recruitment included postings on IBD support group websites and discussion forums including IBDsupport.org, healingwell.com, Reddit, and the Clinical Trials page of the CCF website. In-person recruitment was conducted at a local gastroenterology department, where a physician IBD specialist would mention the study to relevant patients who

Table 1 Participant characteristics

Characteristic	Total sample ($n=140$)	Self help ($n=70$)	Psychoeducation ($n=70$)
Age (M (SD))	35.64 (13.18)	35.69 (13.20)	35.00 (13.25)
Sex (% female)	66	64	67
Race (%)			
Asian	4	4	3
American Indian/Alaskan Native	0	0	0
Black or African American	2	0	4
Hispanic	1	0	3
White	82	84	80
Mixed	2	4	0
Other	2	0	4
Prefer to not disclose	7	8	6
Diagnosis			
Crohn's disease	48	52	45
Ulcerative colitis	33	27	40
Indeterminate colitis	1	1	0
Lymphocytic colitis	1	0	1
Unspecified IBD	17	20	14
Comorbid IBS			
Present	14	16	13
Absent	52	47	56
Unspecified	34	37	31
Flare status			
Present baseline	42	40	44

could then meet with study personnel on site. Subjects who had expressed interest in-person were contacted via email within 24 h. All potential participants could then follow a link to the study Qualtrics site containing the consent form and intake questionnaires.

Inclusion/Exclusion Criteria

Inclusion criteria were comprised of self-report of a prior physician diagnosis of IBD or referral by a physician with physician confirmation of diagnosis. All IBD diagnoses were eligible for the study, including CD, UC, and IBD-Unclassified. Subjects who reported a comorbid IBS diagnosis in conjunction with their IBD diagnosis were also eligible for the study. Participants under the age of 18, and those who did not report being diagnosed with an IBD were excluded. Note that while efficacy trials typically require confirmation that patients truly have the disease of interest, effectiveness trials allow for more heterogeneous patient populations (Singal et al., 2014). Subjects were not excluded for any reason other than lack of prior diagnosis or being under the age of 18.

As part of the IRB-approved protocol, participant's BDI scores were monitored throughout the study at each data-collection timepoint. If participants endorsed a score of either 2 or 3 on item 9 of the BDI (the item regarding suicidality), the PI reached out to them directly to evaluate their safety and determine whether they should be referred for a higher level of care. This happened in only one instance, on the baseline measures, and the participant in question responded with gratitude, and noted that she had a great support system in place and was in the process of reaching out to see a counselor. She was exited from the trial but was allowed access to the self-help book.

Intervention

The intervention was a self-help book based on skills and principles used in CBT, which was specifically designed for patients with IBD (See Table 2). The first module focused on differential diagnosis, the impact of stress on the GI system, and relaxation exercises. The second module introduced the basic cognitive model of stress management. The third module applied the cognitive model to GI symptoms and situations specifically. The fourth module introduced behavioral experiments as ways of testing potentially faulty beliefs. The fifth module encouraged exposure therapy and reducing maladaptive avoidance. The sixth module reviewed evidence-based dietary advice, and touched on the medical treatments, including the role of neuromodulators, as well as including a chapter on ostomies. Throughout the text, numerous IBD-specific clinical examples were provided so

Table 2 CBT self-help workbook

Module	Chapters	Description
Module 1	Chapters 1–3	Introduction to the workbook, differential diagnosis, psychoeducation about the effect of stress on the intestines, relaxation exercises
Module 2	Chapter 4	Discusses "catastrophic cognitions" and introduces cognitive restructuring. Asks participants to complete and practice thought records. Participants describe a negative event, list the thoughts caused by the event, list the feelings caused by those thoughts, and then list a potential alternative explanation for the event that is more objective
Module 3	Chapter 5	Applies cognitive restructuring specifically in the context of GI symptoms and IBD. Participants are asked to complete more thought records
Module 4	Chapter 6	Introduces behavioral experiments. Participants are asked to identify a negative belief regarding their GI symptoms, predict what will happen if that belief is true, test the relevant situation, and compare what actually happens to the prediction
Module 5	Chapter 7	Discusses avoidance behaviors and how and why to eliminate them
Module 6	Chapters 8–11	Discusses diet, medical treatment options, and ostomy considerations. Concludes with final thoughts and summarizes importance of practicing relaxation strategies, objectively looking at negative thoughts, completing behavioral experiments, and eliminating avoidance

that participants would find the material relatable and would have models of how to do the exercises.

The active psychoeducational workbook (PE) was a compilation of information found on the internet that was systematized into focused modules (Table 3). All of the information in the psychoeducational workbook was available online, and the book provided links to all of the websites where the information originated. However, the workbook was carefully curated and organized so that information was presented sequentially, with bridging text between sections. Moreover, the information presented was generally not alarming, in that it contextualized worst-case scenarios (such as surgery or permanent ostomies) and focused primarily on ways for patients with IBD to increase their knowledge base for managing the disease effectively. The psychoeducational workbook covered some material that is *relevant* to depression and anxiety (e.g., being honest with sexual partners about changes to libido and body image, seeking understanding from support groups) but did not include any specific CBT interventions (e.g., relaxation exercises, cognitive interventions to reduce catastrophic cognitions, behavioral experiments or reducing maladaptive avoidance).

The books were equivalent in length and were both divided into six sections for the purposes of the trial. There was a short, entertaining "quiz" at the end of each module, which allowed us to assess whether participants had actually read the material all the way through, thus providing an objective measure of adherence. Participants were given 6 weeks to work through the material. A similar intervention designed for patients with irritable bowel syndrome was also presented in six modules and was completed in 6 weeks by trial participants (Hunt et al., 2014a). While other CBT trials have been longer (e.g., 8 weeks for McCombie et al., 2016, p. 10 weeks for Mikocka-Walus et al., 2015), prior experience suggested that 6 weeks was sufficient time for participants to work through the material.

Participants were allowed to maintain their access to the workbooks for the duration of the trial, just as a self-help book would remain in the person's possession after purchase.

Measures

Harvey-Bradshaw Index (HBI)

The HBI is a five-item questionnaire designed to evaluate disease activity and severity in patients diagnosed with CD (Harvey & Bradshaw, 1980). The HBI targets subjective (e.g., pain) and objective (e.g., mouth ulcers) symptoms in the last 24 h. The measure correlates well ($r = .93$) with the Crohn's Disease Activity Index (CDAI) and is simple to

Table 3 Active psychoeducational control

Module	Chapters	Description
Module 1	Chapter 1	Introduction to IBD: history, types, symptoms, causes, epidemiology
Module 2	Chapter 2	Medical nature of IBD: information on diagnoses, assessments, and treatments
Module 3	Chapter 3	Sexuality and IBD: perspectives on how to foster intimacy and approach the topic of sex with a partner
Module 4	Chapter 4	A look at homeopathic and alternative treatments for IBD: suggests dietary and other natural alternatives
Module 5	Chapter 5	Diet and nutrition: provides dietary suggestions and considerations to manage symptoms
Module 6	Chapter 6	Living with IBD/support for IBD: tips for travel and work as well as thoughts about coping

administer (Vermeire, Schreiber, Sandborn, Dubois, & Rutgeerts, 2010; Yoshida, 1999). Though originally designed to be clinician administered, self-report versions show excellent agreement with clinician administration (Evertsz et al., 2013). The HBI shares some overlap with the abbreviated Powell-Tuck Index which measures self-reported symptom severity in ulcerative colitis (Maunder & Greenberg, 2004), including questions pertaining to general well-being/health, abdominal pain, and number of liquid or soft stools per day. Unfortunately, the authors were unaware of the Powell-Tuck Index when the study was designed. Because the HBI does not specifically assess blood in the stool, anorexia or nausea/vomiting, it may be an underestimate of symptom severity in UC.

Gastrointestinal Symptom Rating Scale (GSRS)

The GSRS is a 13 item self-report measure that evaluates GI symptom severity across five domains. These domains include bloating, diarrhea, constipation, pain, and satiety (Wiklund et al., 2003). Individuals rate their symptom severity on a 7-point Likert scale extending from 0 (Not at all) to 6 (Very Severe). The GSRS has high internal consistency, with Cronbach's alpha varying from 0.74 (pain) to 0.85 (satiety). The scale has high test–retest reliability across the domains (0.55–0.70).

Visceral Sensitivity Index (VSI)

The VSI evaluates gastrointestinal symptom-specific anxiety and hypervigilance (Labus et al., 2004). A 6-point Likert scale ranging from 0 (Strongly Disagree) to 5 (Strongly Agree) is utilized. Validation studies have demonstrated high internal consistency (Cronbach's alpha of 0.93). In addition, the VSI has been shown to possess reliable concurrent, divergent, and discriminant validity (Labus et al., 2004).

Gastrointestinal Cognitions Questionnaire (GI-COG)

The GI-COG is a 16-question inventory that assesses catastrophic gastrointestinal-specific cognitions (Hunt, Ertel, Coello, & Rodriguez, 2014b). Items are rated on a 5-point Likert scale, ranging from 0 (Hardly) to 4 (Very much). The GI-COG has demonstrated excellent internal consistency (Cronbach's $\alpha = 0.92$) and good test–retest reliability ($r = .87$, $p < .001$) (Hunt et al., 2014a, b).

The Short Inflammatory Bowel Disease Questionnaire (SIBDQ)

The SIBDQ, measuring health-related quality of life in patients with IBD, is a short form of the Inflammatory Bowel Disease Questionnaire (IBDQ) (Irvine, Zhou, & Thompson, 1996). The questionnaire uses a 7-point Likert Scale ranging from 1 (All of the time) to 7 (None of the time). It is scored such that higher scores indicate more impaired HRQL. It has moderate test–retest reliability ($r = .65$), and internal consistency (Cronbach's $\alpha = 0.78$).

Spielberger State-Trait Anxiety Inventory (STAI)

The STAI asks individuals to respond to 20 items utilizing a 4-point Likert scale, extending from 1 (Not at all) to 4 (Very much so) (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). The state anxiety version was used in this study, since trait anxiety is unlikely to change during a six-week intervention. The STAI has moderate test–retest reliability ($r = .65$–$.75$) and good internal consistency ($\alpha = 0.86$–0.95).

Beck Depression Inventory II (BDI)

The BDI is a 21-item questionnaire that measures an individual's current depressive symptom severity (Beck, Steer, Ball, & Ranieri, 1996). It has been found to have high internal consistency ($\alpha = 0.91$) and high test–retest reliability ($r = .93$).

Procedure

Once participants were consented and randomized, they were provided links to the respective CBT or PE workbooks. Both workbooks consisted of six modules. To confirm completion of each module, a link that directed the participant to a set of easy, humorous multiple-choice questions could be found at the end of each module. 3 weeks into the program, subjects received an email reminding them to keep progressing with the materials. After 6 weeks, subjects were asked to complete the set of posttreatment questionnaires. Individuals in the immediate treatment group (who had received the CBT Workbook) were sent a final set of questionnaires 3 months later. Individuals in the control group (who had received the PE workbook) were offered the opportunity to cross over to the CBT Workbook after completing the six-week posttreatment questionnaires. Of the subjects who were still actively involved in the trial, (24) 53% elected to cross over. They then had 6 weeks to complete the CBT book, after which they were asked to complete the posttreatment questionnaires again, and then again at three-months post CBT workbook. See Fig. 1 for the consort diagram.

Statistical Analyses

Statistical analyses were performed with the software package IBM SPSS Statistics version 23 (IBM Corporation, Armonk, NY, USA). Analyses included correlation, independent sample t-tests to examine between-group differences

at baseline, paired samples t-tests to examine within group changes over time, and ANCOVAs to examine between-group differences controlling for baseline variables. In addition, multiple imputation was carried out to account for attrition and missing data. The multiple imputation was carried out with the MI module for SPSS, and the resulting imputed data were also subjected to ANCOVAs to examine between-group differences. Results are reported separately for both the completer sample and for the full intent-to-treat sample of all individuals randomized into the trial, with missing data replaced using multiple imputations.

The primary outcomes were the between-group differences at posttreatment on all measures for the CBT group versus the PE group controlling for pretreatment levels. We also examined within group change from pre to post treatment, from pretreatment to 3-month follow-up, and from posttreatment to 3-month follow-up for the immediate treatment group. In addition, for the subset of participants who elected to cross over from the PE workbook to the CBT workbook, we examined incremental gains over the PE workbook and maintenance of gains at three-month follow-up.

Results

Baseline Scores

With the exception of HBI, all baseline scores were acceptably distributed, with absolute skewness values < 1.0. There was a single outlier who reported an inordinate number of diarrhea episodes, thus inflating her HBI score (standardized HBI score at baseline was $z = 4.89$ placing her almost five standard deviations above the mean for the sample). When her data were excluded, the HBI scores were no longer significantly skewed. There were highly statistically significant differences in baseline severity according to recruitment method, with individuals recruited online reporting more distress and impairment across all measures except the HBI [all $t(138) > 3.7$, all $p < .001$]. There were no differences in overall GI symptom severity (on either the HBI or the GSRS) between participants with Crohn's disease and participants with UC, although the HBI may underestimate disease severity for patients with UC. Participants who did not specify the type of IBD they had been diagnosed with reported slightly more distress at baseline than did individuals with Crohn's disease, on the GSRS, the VSI, and the SIBDQ [all $t(89) > 1.96$, all $p \leq .05$], but were not significantly different from individuals with UC.

Attrition

The study had significant attrition in both groups. The overall attrition rate from enrollment to 6-weeks post-test was 37% and to 3-month follow-up was 46%. Within the immediate CBT-treatment group, attrition was 39% and 41%, respectively, and for the PE group, attrition was 36% and 51%, respectively. No baseline scores predicted attrition in the CBT group. However, for the PE group, higher baseline scores on all measures except the HBI were associated with attrition at 6 weeks, and HBI, GSRS, and VSI were associated with attrition at 3 months. See Consort Flow Diagram Fig. 1.

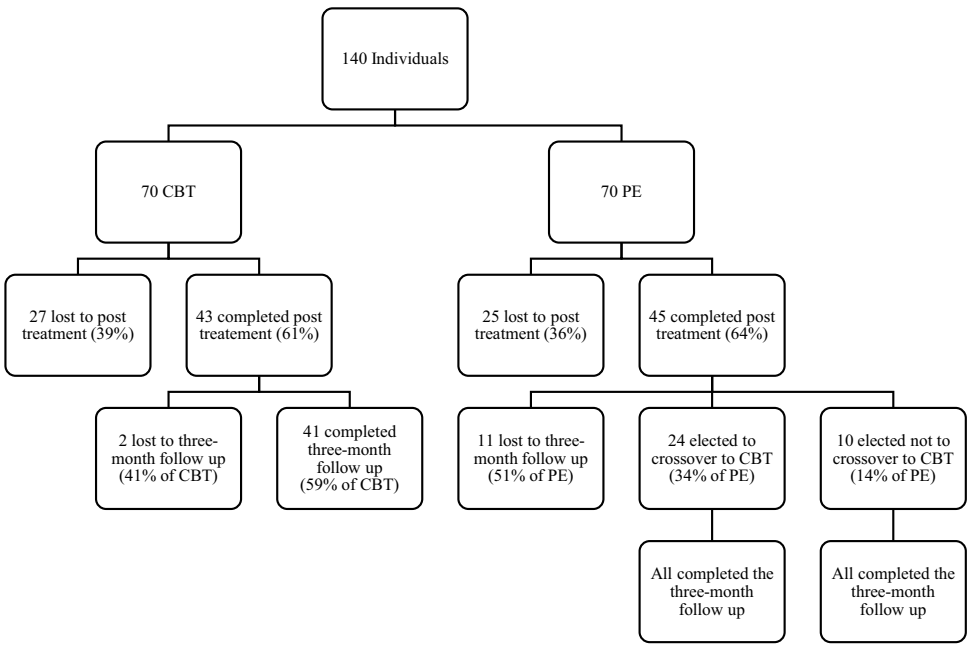

Fig. 1 Consort diagram

Adherence

Adherence was assessed in two ways. First, participants were asked to estimate how much of the treatment they completed (self-reported progress). Second, participant completion of the quizzes at the end of each module was assessed (actual progress). Self-reported and actual progress through the modules had a moderate-to-strong correlation for both treatment groups (PE $r = .44$, $p < .01$; CBT $r = .65$, $p < .001$]. Participants in the PE group reported completing 5.2 modules, but quiz data suggested that they completed an average of 4.5 modules (SD = 2), while participants in the CBT group reported completing 4.8 modules, while quiz data suggested that they completed approximately 3.6 modules (SD = 2.3). The difference in self-reported adherence across groups was not statistically significant, but the difference in actual progress was statistically significant [$t(93) = 1.99$, $p < .05$]. In terms of baseline scores, for the PE group alone, depressive symptoms were marginally negatively correlated with adherence ($r = -.27$, $p = .057$).

Analysis of Treatment Completers

Six-Week Assessment

At the 6-week posttreatment assessment, all outcome measures were acceptably normally distributed except for BDI, which was *slightly* skewed right (absolute skewness of 1.1). In terms of between-group differences, ANCOVAs predicting posttreatment scores by condition, controlling for baseline scores, showed no statistically significant between-group differences on HBI or GSRS, as expected. However, there were statistically significant differences on GICog, SIBDQ, and STAI, all favoring the CBT group [all $F(1,86) > 4.30$, all $p < .05$]. In addition, the CBT group showed nonsignificant trends toward greater improvement on the VSI [$F(1,86) = 2.64$, $p = .108$] and the BDI [$F(1,86) = 3.15$, $p = .08$]. There were no interactions with recruitment source. Individuals recruited online did not respond to treatment differently than those referred by a physician.

In terms of within group differences, the CBT group showed substantial and statistically significant improvement in participants' scores from pre- to posttreatment on the VSI, GICog, SIBDQ, BDI, and STAI [all paired samples $t(42) > 3.31$, all $p < .01$]. There were also nonsignificant numerical improvements from pre- to posttreatment on the HBI [$t(42) = 1.98$, $p = .055$] and GSRS [$t(42) = 1.64$, $p = .11$]. Effect sizes, measured as Cohen's d were typically robust. HBI changed modestly [$d = 0.25$] but all other measures had moderate-to-very large effect sizes, including depression and anxiety scores [all $d > 0.44$], with SIBDQ in particular showing a large effect [$d = 1.30$].

The PE group also experienced statistically significant improvements on the HBI, VSI, GICog, and SIBDQ [all $t(43) > 2.09$, all $p < .05$]. Effect sizes for HBI, VSI, and GICog were all in the small range [d ranged from 0.21 to 0.27]. The effect size for quality of life (SIBDQ) was large [$d = 1.04$]. However, the PE group showed no changes in symptoms of depression or anxiety [both $t(44) < 1.3$, both $p > .15$]. See Table 4 for mean outcome scores for both groups.

Post-cross over

Of the 70 participants randomized to the PE control group, 45 completed the 6-week assessment. Of those individuals, 21 elected not to cross over to the CBT workbook. Of those, only ten individuals completed the 3-month follow-up data. We deemed this sample too small for meaningful comparisons to the original active treatment group or the cross-over group. On the other hand, 24 (53%) chose to cross over to the self-help CBT workbook and completed both the six-week and three-month post-CBT assessments. Looking at within group changes in the cross-over group itself, compared to baseline scores, the combination of psychoeducation and CBT resulted in statistically significant improvement in VSI, GICog, SIBDQ, BDI and STAI [all $t(23) > 2.23$, all $p < .05$]. There was a numerical reduction in disease severity (HBI) as well [$t(23) = 2.05$, $p = .052$]. Compared to the posttreatment scores after completing the psychoeducational book, this group achieved further gains in catastrophizing (GICog) [$t(23) = 2.64$, $p < .05$] but showed only nonsignificant numerical improvement on other measures, including HRQL [$t(23) = 1.57$, $p = .13$], visceral sensitivity [$t(23) = 1.77$, $p = .09$] and anxiety [$t(23) = 1.9$, $p = .07$]. Of note, individuals with the most distress were also the most likely to have dropped out of the study when initially assigned to psychoeducation, thus limiting the variance in the group that remained. Adherence to the CBT book in the individuals who crossed over (2.8 modules completed) was not statistically significantly different from individuals who were assigned to CBT initially (3.6 modules completed).

We also ran the analyses on the combined group of those who read the CBT book initially, and those who were crossed over to it. Looked at this way with a combined sample, comparing scores immediately pre-CBT (which is baseline for the immediate treatment group and is the 6-week posttreatment score for the control group) to scores post-CBT, the sample showed robust and statistically significant gains on all measures [all $t(65) > 2.5$, all $p < .01$] except for the GSRS, which showed numerical but nonsignificant improvement [$t(65) = 1.88$, $p = .065$].

Table 4 Outcome scores by conditions at baseline and posttreatment

	CBT workbook	PE workbook
HBI		
Baseline full sample ($N=140$)	10.21 (5.6)	8.49 (4.28)
Baseline Tx completer ($N=87$)	10.4 (5.9)	7.89 (4.3)
Posttreatment	8.95 (5.5)	7.05 (3.5)
GSRS		
Baseline full sample	23.8 (12)	23.6 (13)
Baseline Tx completer	22.1 (12)	20.7 (12)
Posttreatment	19.5 (14)	19.3 (12)
VSI		
Baseline full sample	44 (20)	44 (17)
Baseline Tx completer	44 (19)	41 (16)
Posttreatment	35 (19)†	36 (16)†
GI-Cog		
Baseline full sample	32 (16)	32 (16.6)
Baseline Tx completer	32 (15)	29 (14.6)
Posttreatment	22 (15)*	26 (15)*
SIBDQ		
Baseline full sample	38 (13)	37 (12)
Baseline Tx completer	37 (12)	34 (11)
Posttreatment	21 (11.6)*	22 (12)*
BDI		
Baseline full sample	20 (12)	19 (12)
Baseline Tx completer	19 (11)	15 (11)
Posttreatment	14 (12)†	14 (11)†
STAI		
Baseline full sample	49 (12.7)	47 (13)
Baseline Tx completer	49 (12)	45 (13)
Posttreatment	43 (12)*	44 (13)*

HBI Harvey Bradshaw Index, *GSRS* Gastrointestinal Symptom Rating Scale, *VSI* Visceral Sensitivity Index, *GI-Cog* Gastrointestinal Cognitions Questionnaire, *SIBDQ* Short Inflammatory Bowel Disease Questionnaire, *BDI* Beck Depression Inventory, *STAI* Spielberger State-Trait Anxiety Inventory

*signifies $p<.05$; †signifies $p\leq.10$ in between-group comparisons for the completer sample

Three-Month Follow-up

At 3-month follow-up, the gains made from the CBT workbook alone were still evident, with all measures still statistically significantly improved from baseline [all $t(40)>2.3$, all $p<.05$], with the exception of the GSRS [$t(40)=1.5$, $p=.13$]. Moreover, most gains were maintained from immediately posttreatment, with all measures showing no significant change at three-months from posttreatment scores [all $t(40)<1.0$, all *ns*] with the exception of the SIBDQ, which did show some loss of gains [$t(40)=7.56$, $p<.001$] although it did not revert to pretreatment levels.

With respect to the individuals who crossed over to the CBT book, they also showed excellent maintenance of most gains from immediately post-CBT to 3 months [all $t(23)<1.12$, all *ns*], with the exception of SIBDQ and the HBI, which both showed some loss of gains [both $t(23)>2.54$, $p<.05$].

We then combined the initial CBT group with the crossover group. Paired-samples *t* tests were carried out comparing baseline scores to scores at 3-month follow-up for all individuals who completed the CBT workbook (including individuals who read the PE book initially, and then crossed over to the CBT book). Scores on all measures remained statistically significantly improved, [all $t(64)>2.58$, all $p<.05$], with the exception of GSRS which was marginally improved [$t(64)=1.97$, $p=.053$]. Effect sizes were all in the small-to-medium range (between 0.24 for GSRS up to 0.59 for the VSI and 0.72 for the GICog).

Changes in disease severity were strongly associated with changes in SIBDQ at 3 months, above and beyond SIBDQ at post CBT treatment [$F(1,64)=15.59$, $p<.001$]. Furthermore, whether or not individuals reported being in flare at 3 months was also significantly associated with SIBDQ at 3 months, over and above SIBDQ at post CBT treatment [$F(2,64)=4.67$, $p<.05$]. Nevertheless, quality of life remained significantly improved over pretreatment baseline, even when disease was flaring. Taken together, these findings suggest that individuals who underwent CBT benefited from psychological resilience in the face of new flares.

Intent-to-Treat Analyses

Multiple Imputations of Missing Data

In order to account for missing data due to attrition and present a true intent-to-treat analysis, we used multiple imputations of missing data. SPSS version 23 allows for multiple imputations using either Markov-Chain Monte Carlo (MCMC) modeling, when the data are missing at random, or monotone imputation strategies to reduce bias when the missing data are not random. Since baseline variables did predict attrition for the PE control group, monotone imputation strategies were employed to reduce bias (IBM, 2012). The program then supports inferential statistics using the pooled data. We set the specifications to a total of ten iterations (Spratt et al., 2010). The imputation regression included sex, age, condition, all baseline measures, and posttreatment assessment variables. Using the pooled data from ten iterations of imputed data, we examined the between-group differences at posttreatment. There were significant between-group differences favoring CBT on the primary outcome measure of SIBDQ [$F(1,1486)=11.87$, $p=.001$]. There were also significant differences favoring CBT on the GI-Cog [$F(1,1486)=18.08$, $p<.001$] and the STAI [$F(1,1485)=9.75$, $p<.01$]. There was a marginally significant difference in BDI scores [$F(1,1485)=3.64$, $p=.057$].

There were no significant differences between groups on improvement on the VSI, the GSRS, or the HBI.

Examining the baseline to three-month follow-up data for subjects in both the CBT group and the PE group who chose to cross over to the CBT book, differences were robust and highly significant, suggesting that people by and large maintained their gains (all $t > 3.3$, all $p \leq .001$).

Discussion

Based on early pilot work on a preliminary intervention workbook, (Hunt et al., 2017), we anticipated that participants in the self-help CBT group would show improvements in health-related quality of life, as well as decreases in anxiety, depression, catastrophizing, and anxiety about visceral sensations compared with baseline at 6-week follow-up. As we expected, participants in the self-help CBT group improved on all of these measures. Indeed, in the full intent-to-treat analysis the CBT group showed significantly greater improvement on HRQL, catastrophizing, anxiety, and (marginally) depression than the PE group. Contrary to our expectations, however, participants in the psychoeducational group *also* received some benefits from the treatment, as they showed statistically significant pre-post improvements in catastrophizing, visceral anxiety, and HRQL.

However, the PE workbook had several shortcomings. First, the people who were most distressed at baseline were the most likely to stop reading it and drop out of the study, whereas baseline distress did *not* predict attrition in the CBT group. Moreover, the PE book did not lead to significant improvement in anxiety and depression symptoms. The finding that the CBT group improved significantly or at least somewhat more than the PE group in both anxiety and depression is not surprising, given that CBT specifically targets these symptoms and is one of the most empirically supported treatments for both anxiety and depression. When participants in the PE group were crossed over into CBT, they experienced significant reductions in both depression and anxiety over baseline, as well as further reductions in catastrophizing over their initial post-psychoeducation scores. This suggests that for the least-distressed patients with IBD, simple psychoeducation that is carefully curated and sequentially presented can be quite helpful at facilitating coping and improving HRQL. For *distressed* individuals, however, psychoeducation may be overwhelming and difficult to engage with, and is clearly insufficient, whereas CBT self-help can be quite effective. Interestingly, this is consistent with the results of the Mikocka-Walus et al.'s (2015) trial which also showed that CBT was the most effective for the subset of more distressed individuals.

At 3-month follow-up, many of the participants' gains appeared to be maintained. Participants in the CBT group maintained or improved their gains in anxiety, depression, catastrophizing, and visceral hypersensitivity. However, participants in both groups lost *some* of the gains they had made in health-related quality of life, while they remained improved over baseline. This result may be related to worsening disease severity and the onset of active flares.

Multiple imputations of missing data yielded similar results, suggesting that both groups improved across the board from pretreatment to baseline, with the CBT group improving significantly more than the PE group on HRQL, anxiety, and catastrophizing, and marginally more on depression. Moreover, from pretreatment to 3-month follow-up, all the participants who received the CBT book showed robust treatment gains over baseline that were maintained, despite some active disease flares. The only domain that showed some loss of gains from posttreatment to three months was HRQL, which was related to worsening disease activity.

Both the CBT self-help book *and* a carefully curated psychoeducational control workbook resulted in significant improvement in psychological distress and HRQL, with the CBT book resulting in somewhat more robust gains, for more distressed people, especially in the domains of anxiety and depression. These observations suggest that self-help interventions can be enormously helpful to individuals with IBD, many of whom may not need the direct face-to-face services of a trained mental health provider, which can often be both expensive and difficult to obtain (Craven, et al., 2018). Moreover, these types of interventions are easy to access and can allow for faster, easier, more effective dissemination of evidence-based and empirically supported treatment to improve HRQL in patients with IBD. This study is the first to show that a purely self-help, stand-alone workbook, with no active therapist interaction or feedback, can be effective for this population.

The current study has several important limitations. The first limitation of this study was that participants who were recruited online did not have a confirmed diagnosis of IBD, but rather reported having been diagnosed with IBD by a physician. However, when patients purchase self-help books, sellers do not require physician confirmation of diagnosis, which enhances the ecological validity and generalizability of the trial, as demanded by an effectiveness trial. Furthermore, about one-quarter of participants were recruited in-person in a local hospital where a physician with expertise in IBD verified their diagnoses. The online sample reported significantly more distress and impairment across all measures at baseline, suggesting that such patients are particularly in need of intervention. Moreover, there were no interaction effects with recruitment source, suggesting that patients recruited online or physician referred responded to treatment equivalently. Thus, we are confident that our intervention is helpful to the population of interest—individuals who understand that they have been diagnosed with IBD by

a physician and are interested in self-help to improve quality of life and distress.

The second limitation was that we did not ascertain whether people were receiving concurrent psychological treatment of some other kind, nor did we prohibit any use or change of use of psychiatric drugs or neuromodulators. It is conceivable that some of the positive changes our participants experienced were due to interventions outside the scope of the study.

The third limitation was our use of the Harvey-Bradshaw Index to measure self-reported disease severity in all the participants, rather than using the HBI in patients with Crohn's disease, and the Powell-Tuck Index (PTI) in patients with ulcerative colitis. We regret that, and will certainly use the appropriate measure in future trials. However, there is actually significant overlap in the item content between the HBI and the PTI, and there were no significant differences in HBI scores between those participants with Crohn's disease and those with UC. If anything, the HBI is likely to be an underestimate of disease severity in UC, since it does not assess bloody stool, anorexia or nausea/vomiting, all of which are included in the PTI.

The fourth limitation is that there was significant attrition (46%). However, attrition is not uncommon for online studies. In fact, a recent meta-analysis of randomized controlled trials conducted entirely on the internet by Mathieu et al. (2013) found the average rate of attrition for online studies to be 47%. This study had far less attrition than the comparable study by McCombie et al. (2016) which reported over 74% attrition from the active treatment arm. A related limitation concerns treatment compliance. Even among the participants who completed the study and filled out the posttreatment questionnaires, many did not fully adhere to the treatment. This lack of adherence was somewhat more problematic for the CBT group. Participants in the PE group completed more modules, which is not surprising considering that this workbook required less active engagement. While the CBT workbook required participants to complete thought exercises and behavioral experiments, participants in the PE group simply had to read factual information.

The surprising efficacy of the psychoeducational workbook suggests that many patients could benefit from simple, but carefully curated educational interventions. A Google search on IBD results in approximately 13 million hits and also quickly leads (within one to three clicks) to graphic and terrifying images of worst-case scenarios (e.g., surgery on diseased tissue, permanent ostomies). Given the overwhelming amount of information on the internet, patients may benefit from structured, sequential education about the most important facts about the disease. While the psychoeducational workbook was surprisingly effective, there did not seem to be any benefit to having both the psychoeducational workbook and CBT when compared with CBT alone, perhaps because the self-help CBT workbook also contains basic psychoeducational information.

CBT was shown to be a useful modality beyond simple psychoeducation. More severe baseline scores predicted higher attrition and lower adherence for the psychoeducation group but *not* for the CBT group, which suggests that CBT is a more helpful treatment approach for those who have greater disease burden and are more psychologically distressed. While psychoeducation appears to have been effective for patients who were less severe at baseline, CBT appears to have been helpful to people regardless of baseline severity. In addition, CBT was found to be helpful in improving anxiety and depression scores, in contrast to psychoeducation which had no influence on these scores.

However, as effect sizes at three-month follow-up were modest, future research should consider other ways to augment treatment efficacy. One obvious route would be to include a few therapist led sessions. This would be less expensive than a full course of in-person CBT, but it has the same problems of access and geographic availability. Another route would be to supplement CBT with mindfulness-based interventions, which have also proven efficacious for patients with IBD (Neilson et al., 2016). Nevertheless, self-help CBT appears to be a promising treatment for distressed patients with IBD, and this study is the first to show that a purely self-help workbook based on CBT strategies can be an effective way to improve HRQL in IBD.

Compliance with Ethical Standards

Conflict of interest Melissa G. Hunt, Paddy Loftus, Michael Accardo, Mary Keenan, Lauren Cohen, and Mark T. Osterman declare that they have no conflicts of interest.

Human and Animal Rights All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki declaration of 1975, as revised in 2000.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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